

Lung Cancer in Women: Present and Future Trends ^{1,2}

Ernest L. Wynder, M.D.,³ Lirio S. Covey, M.A., and Kiyohiko Mabuchi, M.D.,⁴ Division of Epidemiology, Naylor Dana Institute for Disease Prevention, American Health Foundation, New York, New York 10019

SUMMARY—A retrospective study of 108 female lung-cancer patients seen during 1970–72 showed that cigarette smoking was closely associated with epidermoid and oat-cell types of lung cancer, and less strongly with glandular types of lung cancer. Among cigarette smokers of >1 pack/day, a longer history of smoking, earlier starting age, inhalation, and nonfilter cigarette smoking were significantly associated with greater lung-cancer morbidity ratios. Another study of 1839 male and 2213 female control patients showed great differences in various smoking-intensity factors between men and women, but the differences diminished at younger ages. As women adopt cigarette-smoking habits similar to those of men, the death rate from lung cancer in women will continue to increase. However, the level is not expected to attain that presently observed in men, since young women began smoking cigarettes with lower tar-yield (i.e., filters) than did men presently of lung-cancer age.—*J Natl Cancer Inst* 51: 391–401, 1973.

IN A RETROSPECTIVE study of lung cancer in women in 1956, the hypothesis was presented that cigarette smoking would substantially increase the risk of epidermoid lung cancer in women. This was difficult to measure at that time because of the small number of women who had smoked for long periods (1). The possibility that cigarette smoking also increased the risk of lung adenocarcinoma in women could not be eliminated.

Our present study examines the relationship between cigarette smoking and lung cancer in female patients in whom the disease was diagnosed during 1970–72, and reviews recent trends of lung-cancer epidemiology in women. We compared epidemiologic data obtained 15 years apart and formed a hypothesis regarding future trends.

This paper, like the 1956 study, is a review of pertinent literature, a case-control study of lung cancer, and a comparison of smoking habits of men and women.

LITERATURE REVIEW

Two prospective studies of smoking habits reported on lung cancer in women. A study by Hammond (2) of 210 deaths in women due to lung cancer showed a higher mortality ratio among current smokers of all ages (40–74 yr) who smoked 20 or more cigarettes per day (1.76 vs. 1.06 for 1–19

cigarettes/day), who inhaled moderately or deeply (3.70 vs. 1.78 who inhaled slightly or not at all), and who began smoking before age 25 (3.65 vs. 1.70 for those who began after age 25). Hirayama's study (3) of 142,857 Japanese women aged 40 and over included 94 deaths from lung cancer and showed that the mortality from lung cancer was 2.44 times greater for smokers than for non-smokers. Women smoking 20–24 cigarettes per day showed a mortality ratio of 3.14, compared with 2.65 for women who smoked 1–9 cigarettes per day.

Results from retrospective studies of >100 women with lung cancer are presented in table 1 (4–7). Cigarette-smoking history and the number

¹ Received March 6, 1973; accepted April 20, 1973.

² Supported by Public Health Service contract NIH-70-2087 from the National Cancer Institute.

³ Address reprint requests to: Dr. Ernest L. Wynder, 1370 Avenue of the Americas, New York, N.Y. 10019.

⁴ We thank Dr. Edward J. Beattie, Jr., Memorial Sloan-Kettering Cancer Center; Dr. Lester Breslow, University of California, Los Angeles; Dr. Walter J. Burdette and Dr. Rulon W. Rawson, M.D. Anderson Hospital and Tumor Institute, Houston, Texas; Dr. Sherman Kupfer, Mt. Sinai Hospital, New York City; Ms. Evelyn Peck, St. Luke's Hospital Center, New York City; Ms. Dorothy Ward, Metropolitan Hospital, New York City. We also thank Ms. Dorothy Lim and Ms. Esther Moore, New York City; Ms. Betty Henry, Houston, and Ms. Betty Gould, Los Angeles, who conducted the interviews.

smoked daily consistently showed a relationship to lung cancer. Attempts to measure the independent effect of other smoking-intensity factors (e.g., duration of cigarette-smoking habits, starting age, and depth of inhalation) have been largely unsuccessful because of the limited population size and the interrelationship between these factors and the current number of cigarettes smoked.

A study by Haenszel and Taeuber (8) on a 10% sample of all lung-cancer deaths in white females in the United States during 1958 and 1959 demonstrated higher mortality ratios, increasing for cigarette smokers with the number smoked (8). Comparison of mortality of males and females who smoked one or more packs of cigarettes daily showed that lung-cancer rates for males were 4 times higher than for females. Haenszel and Taeuber suggested that more accurate measures of "effective exposure," as age when smoking was started, butt length, inhalation practices, and tar content, might resolve or greatly diminish the disparities in risks between male and female smokers.

CASE-CONTROL STUDY

Methodology

The study group of 116 women with lung cancer were interviewed between February 1970 and July 1972 in the following hospitals: Memorial Sloan-Kettering Cancer Center, St. Luke's Hospital, Mt. Sinai Hospital, and Metropolitan Hospital in New York City; UCLA Hospital and USC-LA Medical Center in Los Angeles, California; and M.D. Anderson Hospital and Tumor Institute in Houston, Texas. Our data were based only on 108 confirmed histologic determinations, which were performed by the pathology departments of the hospitals where the patients were interviewed.

The control group comprised women hospitalized with diseases other than those designated as tobacco-related (9), and they were interviewed within the same periods and at the same hospitals as the study cases. Four controls matched for age, race, and hospital to each histologically confirmed lung-cancer case were randomly drawn from a data file of 2753 female controls.

A questionnaire covering demographic and background information and a detailed smoking history was administered by interviewers who were trained in New York City. Completed questionnaires mailed back to New York from California and Texas were edited and coded in the New York office. Data were entered into a CDC 1700 computer to generate the basic frequency tables.

For each variable, the standard morbidity ratio (SMR) was calculated by dividing the observed number of cases in a category by the expected value. Expected values were obtained by applying the distribution of controls by a given variable to the corresponding total number of cases. The standard error determined statistical significance of the SMR. The significance of the difference between levels of smoke-intensity factors was evaluated by the *t* distribution. Differences in socioeconomic variables between cases and controls were evaluated by comparing observed and expected numbers.

Results

Histologic evaluation.—Of the total group, 59 (51%) women had epidermoid lung cancer, 44 (38%) had adenocarcinoma, and 5 (4%) had anaplastic lung cancer; 8 unclassified cases were excluded from the analysis. The epidermoid and anaplastic patients were designated Kreyberg group I, and all others constituted Kreyberg group II. The 51% epidermoid cancer in this series differed from the 1956 study, in which we reported that 32% of the women had this cell type of lung cancer (1).

Age distribution.—The median ages were 53.5 years for Kreyberg I and 55.0 years for Kreyberg II (table 2). Both groups showed peak modalities for the age group 50–59 years, and almost 90% of both groups experienced the disease between the ages of 40 and 69.

Socioeconomic variables.—The observed and expected numbers of patients by education, occupation, religion, and place of residence (in childhood, adolescence, and adulthood) are presented for smokers (table 3). No significant differences were found between cases and controls in any category. The slightly smaller-than-expected number of Jewish Kreyberg I cases may have reflected the fewer cigarettes smoked by Jewish women than other religious groups. The slightly larger-than-expected number of Jewish Kreyberg II cases was in agreement with other studies (10, 11), but the difference was not significant.

History of cigarette smoking.—Women who have ever smoked cigarettes comprised 92% of the 64 Kreyberg I cases, 73% of the 44 Kreyberg II cases, and 48% of the controls. The differences were significant both between the Kreyberg I cases and controls ($\chi^2=4.27$, $P<0.001$), and

TABLE 1.—*Smoking data from 5 case-control studies on lung cancer in women*

Author(s) country, & year (reference)	Case: control ratio	Method of data collection	Percent with history of cigarette smoking			Percent of heavy smokers†			Definition of heavy smoker
			Kreyberg group I*	Kreyberg group II †	Control	Kreyberg group I*	Kreyberg group II †	Control	
Wynder et al., U.S.A., 1956 (1)	105:1304	Interviews and ques- tionnaire mailed to close relatives or friends.	62	29	34	45	8	3	20 cigarettes +/ day.
Haenszel and Shimkin, U.S.A., 1958 (4)	158:339	Interviews by resi- dents, social workers, secretaries.	57	33	30	32	28	13	20 cigarettes +/ day.
Doll and Hill, Eng- land, 1952 (5)	108:108	Interviews by almoners.	59	50	89-95	22	40 [§]	2-16 [§]	25 cigarettes +/ day.
Stokes, England, 1957 (6)	255:1517	Interviews with relatives.	42		19	41		20	100 cigarettes +/ wk.
Wicken, N. Ireland 1966 (7)	151:151	Interviews with relatives.	42		20	29		17	23 cigarettes/day.

*Patients with epidermoid and anaplastic lung cancer.

†Patients with lung cancer other than epidermoid or anaplastic types.

‡Values are based on total number of smokers, unless otherwise specified.

§ Based on less than 10 in the category.

|| Value is for both Kreyberg groups I and II.

2063631164